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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,138	08/28/2000	Shigeru Kinoshita	KINOSHITA3	9673
1444	7590	02/04/2004	EXAMINER	
BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303			HUI, SAN MING R	
			ART UNIT	PAPER NUMBER
			1617	15

DATE MAILED: 02/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/623,138

Applicant(s)

KINOSHITA, SHIGERU

Examiner

San-ming Hui

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11, 14, 15, 17, 19 and 20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11, 14, 15, 17, 19 and 20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- ☐ Interview Summary (PTO-413) Paper No(s). _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Applicant's amendments filed November 22, 2003 have been entered.

The outstanding rejection under 35 USC 112, first paragraph is withdrawn in view of the amendments filed November 22, 2003.

Claims 11, 14, 15, 17, 19 and 20 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 11, 14-15, 17, and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paul (Fundamental Immunology, 3rd ed., 1993, Raven Press, page 119-121), Niederkorn et al. (Abstract of Reg. Immunol., 1989 ; 2(2) : 83-90), Dam et al. (Journal of Investigational Dermatology Symposium proceedings; 1996;1(1):72-77) and Muller et al. (Journal of Investigational Dermatology Symposium proceedings; 1996;1(1): 68-71) in view of Itoh et al. (WO96/29079, the English translation, Patent US 6,248,732, is also provided), and Hingorani et al. (Drugs 1995; 50(2); 208-221), references in the previous office action.

Paul teaches Langerhans cells (LC) is an antigen presenting cells that is highly effective in presenting antigen to T cells (See page 120, col. 1). Paul also teaches that

IL-1 increases the antigen presenting function of LC to T cells (See page 120, col. 1, fifth paragraph).

Nieder Korn et al. teaches that LC is present in corneal epithelium and could migrate to the central cornea upon irritants or the presence of IL-1 (See the abstract).

Dam et al. also teaches calcitriol or calcipotriol inhibit $\text{TNF-}\alpha$, a factor which can induce migration of LC, which is a type of antigen presenting cell (See page 76, col. 1, second paragraph). Dam et al. teaches calcitriol and calcipotriol are useful to suppress the number of LC when applied topically (See particularly page 72, col. 2, last paragraph). Dam et al. also teaches calcitriol and calcipotriol suppress the T-cell proliferation (See page 75, col. 2, first paragraph).

Muller et al. teaches the calcitriol inhibits the production of interleukin-1 at a presecretory level such as reducing the levels of interleukin-1 α mRNA, which is known to activate lymphocytes (See page 68, col.2, third paragraph).

The references do not expressly teach calcitriol is in a form of ophthalmic solution. The references do not expressly teach calcitriol is useful in treating keratoconjunctivitis, phlyctenular keratitis, or corneal infiltration. The references do not expressly teach calcitriol is useful in a method to inhibit interleukin-1 production in cornea epithelium and thereby treat ocular inflammation.

Itoh et al. teaches that calcitriol can be formulated into an ophthalmic composition (See See particularly col. 11, line 5-10).

Hingorani et al. teaches atopic keratoconjunctivitis is a T-cell inflammation prominent disorder (See particularly abstract). Hingorani et al. also teaches atopic

keratoconjunctivitis may lead to infiltration and corneal involvement such as epithelial keratitis (See particularly page 210, col. 1, last paragraph).

It would have been obvious to one skill in the art when the invention was made to employ calcitriol, in ophthalmic solution dosage form, in a method to treat keratoconjunctivitis, phlyctenular keratitis, or corneal infiltration. It would have been obvious to one skill in the art when the invention was made to employ calcitriol in a method to inhibit interleukin-1 production in cornea epithelium and thereby treat ocular inflammation, which is the obvious therapeutic benefit herein recited.

One of ordinary skill in the art would have motivated to employ calcitriol, in ophthalmic solution dosage form, in a method to treat keratoconjunctivitis, phlyctenular keratitis or corneal infiltration. It is known that calcitriol inhibits the production of LC migration inducing agent, TNF- α . Employing agents that can block the LC migration, such as calcitriol, to the inflammation site, such as in the cornea, and treating keratoconjunctivitis would be reasonably expected to be useful. In addition, the cited prior art provide additional motivation to employ calcitriol in the instant treatment method because it is known that atopic keratoconjunctivitis is a T-cell inflammation prominent disorder and may lead to infiltration and corneal involvement such as epithelial keratitis. Therefore, employing any T-cell proliferation inhibitor, including calcitriol, would have been reasonably expected to treat keratoconjunctivitis and keratitis, including phlyctenular keratitis or corneal infiltration, thereby.

Furthermore, one of ordinary skill in the art would have motivated to employ calcitriol in a method to inhibit interleukin-1 production in cornea epithelium and thereby

treat ocular inflammation because calcitriol is known to inhibit the production of interleukin-1 α at a presecretory level by reducing the level of interleukin-1 α mRNA. One of ordinary skill in the art would therefore reasonably expect calcitriol be useful in inhibiting the production of interleukin-1 and reducing the function of LC and LC induced activation of T cells, thereby decreasing the inflammation response and treating ocular inflammation. Examiner notes that although the cited prior art do not teach the recited properties of calcitriol, i.e., treat ocular inflammation without lowering transparency of the cornea, such properties must be present in the compounds since the compounds and its properties are not separable.

Response to Arguments

Applicant's arguments filed November 22, 2003 averring the cited prior art's failure to teach treat ocular inflammation without lowering transparency of the cornea have been fully considered but they are not persuasive. As discussed above, products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada* 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. In the instant case, calcitriol is considered to have such intrinsic properties, absent evidence to the contrary.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

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San-ming Hui
Patent Examiner
Art Unit 1617


SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

2/2/04